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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/669,298 09/25/00 AHMAD

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EXAMINER

ART UNIT

PAPER NUMBER

1624

DATE MAILED:

09/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

**Office Action Summary**

Application No.

09/669,298

Applicant(s)

AHMAD ET AL.

Examiner

Hong Liu

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 5, 11, 21, 23 and 32-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-4, 6-10, 12-20, 22, 24-27 and 31 is/are rejected.
- 7) ☐ Claim(s) 28-30 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other:  |

### **DETAILED ACTION**

Claims 1-62 are pending in this application.

#### ***Election/Restrictions***

Applicant's election of Group IV in Paper No. 5 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement is deemed proper and therefore made FINAL. Claims 5, 11, 21, 23, and 32-62 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Applicants are expected to limit the claims in the scope of the elected subject matter.

#### ***Specification***

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

#### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-4, 6-10, 13-20, 22, 24-27, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation of compounds wherein R1 is heteroaryl and Z is imidazole, does not reasonably provide enablement for preparation and use of compounds wherein R1 and Z are other than heteroaryl and imidazole, respectively. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein Z can be an unsubstituted or substituted, single or fused, heteroaryl group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional "Na/H exchange inhibitors" which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein R1 is monocyclic heteroaryl and Z is substituted imidazole have been made.

Furthermore, no biological testing data is provided the instantly claimed compounds. Examples should be of sufficient scope as to justify the scope of the claim. The definitions of the various R variables embrace many structurally divergent groups not represented at all in testing

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since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the “working examples” fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See *In re Fouch*, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability” have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 13, 22, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- 1). The use of heteroaryl" in the definition of Z is unclear to the array of heteroatoms, size of the rings, as well as nature of atoms as ring members. See In re Wiggins 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.
- 2). "Optionally substituted" throughout claim 1 is unclear as to the nature and number of substituent(s) intended.
- 3). In claims 13, 22, and 24, it is unclear what the zigzag symbol stands for. Does it stand for Z. Clarification is required.

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-10, 12-19, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Even et al. Chem Abstract 128: 244047. The instantly claimed compounds read on

the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds, i.e., the corresponding R1 is H or heteroarylcarbonyl, Z is imidazole. *overcome*

Claims 1-4, 6-10, 12, 13, 15-19, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Ganellin et al. Chem Abstract 123: 198692. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds, i.e., the corresponding R1 is pyridine and Z is imidazole. *not overcome*

Claims 1, 2, 4, 6, 8-10, 12, 15, 16, 17, 22, 24, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Corbel et al. Chem Abstract 126: 259445. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds, i.e., the corresponding R1 is alkyl and Z is imidazole. *overcome*

Claims 1, 2, 4, 6, 10, 12, 14-16, 22, 24, 25, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Schunack et al. Chem Abstract 80: 82801. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds. *overcome*

Claims 1, 2, 4, 6-10, 12, 14-16, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Arrang et al. (US Patent 4,707,487). Arrang teaches the compounds and composition of the instant invention (see Examples and compounds in Table 1). *not overcome*

Claims 1-4, 6-10, 12, 13, 15-18, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jagham et al. (US Patent 5,280,030). Jagham teaches the compounds and composition of the instant invention (see Examples and compounds in Table 1 in col. 9). *not overcome*

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Claims 1, 2, 4, 6, 8-10, 12, 15, 16, 22, 25, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jagham et al. (US Patent 5,434,169). Jagham teaches the compounds and composition of the instant invention (see compounds in the Table, cols. 4-10).

Claims 1, 2, 4, 6, 8-10, 12, 14, 16, 22, 24, 25, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Durant et al. (US Patent 5,663,350). Durant teaches the compounds and composition of the instant invention (see Example and compounds in the Table, cols. 15 and 16).

Claims 1, 2, 4, 6, 10, 12, 14-16, 22, 24, 25, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Lange et al. Chem Abstract 124: 965601. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4, 6-10, 12, 14-16, 22, 24, 25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arrang et al. (US Patent 4,707,487). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I,



Col. 1 wherein R<sub>1</sub> is hydrogen, methyl or ethyl, R is hydrogen or R<sub>2</sub> wherein R<sub>2</sub> is alkyl, a 3-(1-benzimidazolonyl)propyl group or a group of formula  $-(CH_2)_n-X-phenyl-R_3$ , wherein n is 0-3, and X is a bond or a heteroatom or CH-phenyl, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. V. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Claims 1-4, 6-10, 12-19, 22, 24, 25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jagham et al. (US Patent 5,280,030). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, Col. 1 wherein the substituents corresponding to R<sub>1</sub> of the present application is benzimidazole, benzathiazole, or benzoxazole, Z is hydrogen or fluorine, and the substituent corresponding to Z

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of the present application is substituted or unsubstituted imidazole, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Claims 1, 2, 4, 6, 8-10, 12, 14-16, 22, 25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jagham et al. (US Patent 5,434,169). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, Col. 1 wherein R represents hydrogen or alkyl, Ar is optionally substituted phenyl or a heterocyclic group, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the

reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

Claims 1, 2, 4, 6, 8-10, 12, 14, 16, 22, 24, 25, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Durant et al. (US Patent 5,663,350). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, Col. 6 wherein Z is R<sub>2</sub> or C(X)-R<sub>1</sub> wherein X can be O, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus.

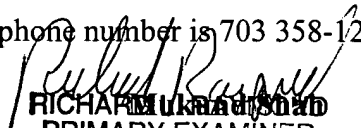
***Claim Objections***

Claims 28-30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. None of the prior art of record, nor a search in the pertinent art area teaches the exact species of the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Liu whose telephone number is 703 3065814. The examiner can normally be reached on 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703 308 4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703 308-4556 for regular communications and 703 3084734 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 358-1235.

  
RICHARD MUKUND SHAH  
PRIMARY EXAMINER  
Supervisory Patent Examiner  
ART UNIT 1624  
Art Unit 1624

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September 23, 2001